UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,581	04/30/2002	Mortimer M. Civan	L-2070	1751

67283 7590 02/12/2009

MONTGOMERY, MCCRACKEN, WALKER & RHOADS, LLP
123 SOUTH BROAD STREET
AVENUE OF THE ARTS
PHILADELPHIA, PA 19109

EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
02/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/009,581
Filing Date: April 30, 2002
Appellant(s): CIVAN ET AL.

Evelyn H. McConathy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 12, 2008 appealing from the Office action mailed January 11, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appellant's statement of the status of amendments after final rejection contained in the brief is incorrect. Appellant states that no amendments have been made to the claims since Appellants' response dated October 31, 2007. The date appears to be incorrect. The claim set entered into the case on November 2, 2007 was amended. A non-final rejection was issued in response to this claim set on January 11, 2008.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is substantially correct. Appellant states that identifying and characterizing a sodium/proton exchanger as the antiport permits strategies to be developed to use drugs at very low, focused concentrations for preventing, modulating or regulating intraocular pressure and most

particularly for treating or reducing elevated intraocular pressure (see page 9, last paragraph of brief). These assertions are not found in the instant claims.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

NEW GROUND(S) OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 115 and 116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Regarding claims 115 and 116, Appellant is claiming that an anion is transferred into the ciliary epithelial cells of the aqueous humor to block native chloride channels (claim 115) and that the anion comprises cyclamate (claim 116). These claims depend from claim 108 drawn to a method for regulating salt uptake or release by ciliary epithelial cells of the human eye by controlling or modulating the function of one or more antiports of the aqueous humor, a modulating amount of a

pharmaceutical composition consisting essentially of an NHE inhibitor. Upon review of the instant specification for an indication as to where anion/cyclamate comes from, Figure 7 indicates that the voltage dependent change in current is produced by selective A3 subtype adenosine agonist (IB-MECA) when most of the external chloride has been replaced by either aspartate or cyclamate. There is no indication that this IB-MECA is a NHE inhibitor, consequently the claims lack written description. Further, Claim 108 contains the transitional phrase "consisting essentially of" which limits the scope of the claim to the specified material or steps and those that do not materially affect the basic and novel characteristics of the claimed invention. It does not appear that there is an IB-MECA, anion or cyclamate claimed in instant claim 108. The addition of the anion or cyclamate appears to be a step or material that would materially affect the basic and novel characteristics of the claimed invention.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

4,950,591	Cherksey	8-1990
5,559,151	Adorante et al.	9-1996
5,585,401	Brandt et al.	12-1996

Drug Facts and Comparisons, 1994 edition, Wolters Kluwer Co., pages 2287-2292

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 101, 115 and 116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, "precursor prostaglandins" (present claim 101) is a concept that was not present in the specification as originally filed. Appellants are advised that the issue here is not whether particular instance of a prostaglandin precursor, but rather whether the concept of other prostaglandin precursors other than latanoprost" was present in the specification as originally filed.

The specification as originally filed contains the following disclosures concerning a prostaglandin inhibitor:

(i) "another new type of drug, precursor prostaglandin compounds (e.g., latanoprost) are also in current use". (page 3, lines 27-28).

The above disclosure, however, does not provide adequate support for any prostaglandin precursor. Prostaglandin precursors include essential fatty acids, such as arachidonic acid, linoleic acid, eicosapentanoic acid and dihomogammalinoleic acid. There does not seem to adequate support in the specification for any of these prostaglandin precursors.

An Appellant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The Examiner is guided in his opinion that Appellant has not adequately described the presently claimed subject matter by the MPEP at § 2163 - 2163.05. In particular, while Appellant's specification as originally filed contained a specific reference to latanoprost as being one example of a prostaglandin precursor but such does not entitle Appellants to now claim all prostaglandin precursors because such represents a subgenus that was not previously set forth or one that would have been immediately envisaged by one skilled in the art from the specification as originally filed. "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996)"(emphasis added), see MPEP § 2163(I)(A). Also, "See also *In re Smith*. 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ('Whatever may be the viability of an inductive-deductive approach to

arriving at a claimed subgenus, it cannot be said that such a subgenus is necessarily described by a genus encompassing it and a species upon which it reads.' (emphasis added)).", see MPEP § 2163.05(II).

Considering the teachings provided in the specification as originally filed, the Examiner finds that Appellants have failed to provide the necessary teachings, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Appellants had possession of the concept of a "precursor prostaglandin".

Regarding claims 115 and 116, Appellant is claiming that an anion is transferred into the ciliary epithelial cells of the aqueous humor to block native chloride channels (claim 115) and that the anion comprises cyclamate (claim 116). These claims depend from claim 108 drawn to a method for regulating salt uptake or release by ciliary epithelial cells of the human eye by controlling or modulating the function of one or more antiports of the aqueous humor, a modulating amount of a pharmaceutical composition consisting essentially of an NHE inhibitor. Upon review of the instant specification for an indication as to where anion/cyclamate comes from, Figure 7 indicates that the voltage dependent change in current produced by selective A3 subtype adenosine agonist (IB-MECA) when most of the external chloride has been replaced by either aspartate or cyclamate. There is no indication that this IB-MECA is a NHE inhibitor, consequently the claims lack written description. Further, Claim 108 contains the transitional phrase "consisting essentially of" which limits the scope of the claim to the

specified material or steps and those that do not materially affect the basic and novel characteristics of the claimed invention. It does not appear that there is an IB-MECA, anion or cyclamate claimed in instant claim 108. It is unclear to the Examiner where the cyclamate, that blocks the chloride channels, would come from.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 94-96, 102 and 105-107 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cherksey U.S. Patent No. 4,950,591.

Cherksey teaches amiloride is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27). Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders (column 2, lines 5-10). The amiloride derivatives are useful when applied topically for the treatment of glaucoma (column 3, line 66 to column 4, line 3 and column 5, lines 42-47).

Claims 94 and 102-105 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Drug Facts and Comparisons (1994).

Page 6 of Appellant's instant specification identifies beta-blockers as NHE inhibitors (see page 6, lines 23-29, see also page 13, lines 11-26).

Drug Facts and Comparisons teach timolol, a beta-blocker, to be employed to reduce elevated and normal intraocular pressure with or without glaucoma (page 2287). The mechanism appears to be a reduction of aqueous production, and a slight increase in outflow facility. Regarding claims to regulating salt uptake or release by ciliary epithelial cells of the human eye by modulation of the antiports, this action is considered to be inherent. Appellants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in Ex *parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well-known compounds or compositions. It is now well-settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975)." In the

instant application, Appellants' failure to distance the proffered claims from the anticipated **prophylactic** utility renders such claims anticipated by the prior inherent use. Regarding administration of the composition to the ciliary epithelial cells of the aqueous humor, there does not seem to be any description of how one would bypass administering an eyedrop to an eye to administer said compositions to the ciliary epithelial cells of the aqueous humor. A prior art reference may anticipate without disclosing a feature of the claimed invention, if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991). Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. E.g., *In re Cruciferous Sprout Litig.,* 301 F.3d 1343, 1351 (Fed. Cir. 2002); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where the result is a *necessary consequence* of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."); Atlas Powder, 190 F.3d at 1348-49 ("Because 'sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention. An inherent structure, composition, or function is not necessarily known."). In the instant case, the unappreciated anticipation also does not require recognition. Appellant claims to have discovered the method of modulating aqueous secretion by modulating the antiports of the aqueous humor. Since the pharmaceutical compositions claimed by Appellant produced the claimed modulation of aqueous secretion, the discovery of the modulation of the antiport is

inherent. In the context of the accidental anticipation, beta-blockers, such as timolol, do not accidentally modulate the antiport when the pharmaceutical composition is applied to a patient in need of treatment. The antiport necessarily and inevitably is modulated when the beta-blocker is applied and does not require a skilled artisan to recognize the inherent characteristic in the prior art that anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Appellant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 94-96, 99-110, 112 and 113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adorante et al. U.S. Patent No. 5,559,151 and Cherksey U.S. Patent No. 4,950,591.

Adorante et al. teach pharmaceutical compositions and methods for treating glaucoma and/or ocular hypertension comprising administering to the mammalian eye an agent such as 4,4'-diisothiocyantostilbene-2,2'-disulfonate (DIDS) (see column 5, lines 10-18). It is noted that Adorante et al. identifies this agent as a chloride channel blocker. The identification of the agent DIDS as a chloride channel blocker does not detract from the teaching that this agent, when it is administered to the mammalian eye, treats ocular hypertension/glaucoma because the chloride-dependent ion flux pathways will inhibit aqueous humor formation and thus, lower intraocular pressure (IOP) (column 5, lines 45-49). Adorante further teaches that drugs currently utilized in the treatment of glaucoma include, *inter alia*, miotics, sympathomimetics, beta blockers, alpha-2-agonists and carbonic anhydrase inhibitors. In vitro (see example, column 5) and in vivo (see claim 1) use are clearly disclosed.

Adorante et al. fails to teach coadministration of NHE/NHE-1 inhibitors.

Cherksey teaches amiloride (NHE inhibitor/NHE-1 inhibitor) is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27). Amiloride and derivatives are

capable of regulating membrane transport, cellular volume or cellular pressure disorders (column 2, lines 5-10). The amiloride derivatives are useful when applied topically for the treatment of glaucoma (column 3, line 66 to column 4, line 3 and column 5, lines 42-47).

As stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

It would have been made obvious to one of ordinary skill in art at the time it was made to employ two agents well-known to treat glaucoma/ocular hypertension together to treat the very same condition. Adorante et al. teach that DIDS treats glaucoma and/or ocular hypertension by inhibiting aqueous humor formation and thus, lowering IOP. Cherksey teaches amiloride (NHE inhibitor/NHE-1 inhibitor) is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27). Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders. One would have been motivated to combine these treatments motivated by the reasoned expectation of producing a composition, which is effective in comprehensively treating persons suffering from elevated intraocular pressure and glaucoma.

Regarding claims drawn to regulating salt uptake or release by ciliary epithelial cells of the human eye or eye of an animal having a trabecular meshwork (network) by controlling or modulating the function of one or more antiports of the aqueous humor ciliary epithelial cells by administering to the ciliary epithelial cells of the aqueous humor a modulating amount of a pharmaceutical composition consisting essentially of an NHE inhibitor, Appellants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well known compounds or compositions. It is now well settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful.

Claims 94-98, 102-110, 112 and 113 rejected under 35 U.S.C. 103(a) as being unpatentable over Brandt et al. U.S. Patent No. 5,585,401 and Cherksey U.S. Patent No. 4,950,591.

Brandt et al. teach the administration of compounds that inhibit the function of Na^{+}-K^{+}-$2Cl^{-2}$ cotransporter mechanism (symport) (see abstract) such as bumetanide for topical administration (column 6, lines 30-43). It has been discovered that the

trabecular meshwork of the mammalian eye regulate cell volume and fluid transport by means of the Na^{+}-K^{+}-$2Cl^{-2}$ cotransporter mechanism. Compounds that substantially inhibit operation of this mechanism also increase the outflow of the ocular fluids, thus lowering intraocular pressure for treatment of ocular hypertension and glaucoma (column 6, lines 15-29).

Brandt et al. fails to teach coadministration of NHE/NHE-1 inhibitors.

Cherksey teaches amiloride (NHE inhibitor/NHE-1 inhibitor) is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27). Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders (column 2, lines 5-10). The amiloride derivatives are useful when applied topically for the treatment of glaucoma (column 3, line 66 to column 4, line 3 and column 5, lines 42-47).

As stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

It would have been made obvious to one of ordinary skill in art at the time it was made to employ two agents well-known to treat glaucoma/ocular hypertension together to treat the very same condition. Adorante et al. teach that DIDS treats glaucoma and/or

ocular hypertension by inhibiting aqueous humor formation and thus, lowering IOP. Cherksey teaches amiloride (NHE inhibitor/NHE-1 inhibitor) is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27). Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders. One would have been motivated to combine these treatments motivated by the reasoned expectation of producing a composition which is effective in comprehensively treating persons suffering from elevated intraocular pressure and glaucoma. Regarding administration of the composition to the ciliary epithelial cells of the aqueous humor, there does not seem to be any description of how one would bypass administering an eyedrop to an eye to administer said compositions to the ciliary epithelial cells of the aqueous humor. A prior art reference may anticipate without disclosing a feature of the claimed invention, if that missing characteristic is necessarily present, in the single anticipating reference. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991).

Regarding claims drawn to regulating salt uptake or release by ciliary epithelial cells of the human eye or eye of an animal having a trabecular meshwork (network) by controlling or modulating the function of one or more antiports of the aqueous humor ciliary epithelial cells by administering to the ciliary epithelial cells of the aqueous humor a modulating amount of a pharmaceutical composition consisting essentially of an NHE inhibitor, Appellants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation

for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well known compounds or compositions. It is now well settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the instant application, Appellants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

(10) Response to Argument

Regarding the lack of written description of claim 101, Appellant states that the specification where it refers to "latanoprost" as "another new type of drug...also in current use" and one of ordinary skill in the art would therefore, as a part of his/her full knowledge, be familiar with such drugs if they are in current use and would know which drugs are being referred to as a prostaglandin precursor for the stated purpose. In response, it is well established that the specification teaches an invention, whereas the claims define the **right to exclude**. *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 [227 USPQ 577] n.14 (Fed. Cir. 1985). Appellant has not provided adequate support for all prostaglandin precursors. The category of prostaglandin precursors includes essential fatty acids, such as arachidonic acid, linoleic acid, eicosapentanoic acid and dihomogammalinoleic acid. There does not seem to adequate support in the specification for any of these prostaglandin precursors. Appellant has stated that he does not limit the claimed pharmaceutical composition to "only" latanoprost, and are not required to do so by law. In response, appellant does not have adequate support in the instant specification of any precursor prostaglandins, other than latanoprost, thus a claim drawn to this broad class lacks written description for the prostaglandin precursors that are included in this category, such as the essential fatty acids, arachidonic acid, linoleic acid, eicosapentanoic acid and dihomogammalinoleic acid, but are not described in the specification. The Federal Circuit has explained that a specification cannot always support expansive claim language and satisfy the requirements of 35 U.S.C. 112 "merely by clearly describing

one embodiment of the thing claimed." *LizardTech v. Earth Resource Mapping*, Inc., 424 F.3d 1336, 1346, 76 USPQ2d 1731, 1733 (Fed. Cir. 2005). The issue is whether a person skilled in the art would understand Appellant to have invented, and been in possession of, the invention as broadly claimed.

Claims 94-96, 102 and 105-107 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cherksey U.S. Patent No. 4,950,591.

Appellant states that Cherksey's claims are solely for the use of the isolated peptide as a diagnostic and experimental tool, whereas Appellant's invention neither teaches, nor claims a method for regulating the sodium channel or its role in aqueous humor formation. In response, The Examiner directs Appellant's attention to *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for **all** they contain." A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Further, *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab,LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005) (reference disclosing optional inclusion of a particular component teaches

compositions that both do and do not contain that component). Consequently, this argument does not raise an issue of material fact.

Appellant states that his invention neither teaches, nor claims a method for regulating the sodium channel or its role in aqueous humor formation. In response, claim 94 is drawn to a method for **regulating intraocular pressure** by administering a pressure modulating amount of **at least one sodium-hydrogen exchange inhibitor**. The instant specification teaches that "the modulators of the antiports are beta blockers, e.g., as timolol, amiloride analogs, e.g., amiloride or ethyl-isopropyl-amiloride and other compounds, e.g., cariporide." (page 6, lines 23-26) Where an explicit definition is provided by the Appellant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings."). Since Cherksey teaches amiloride is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27) and Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders (column 2, lines 5-10). The amiloride derivatives **are useful when applied topically for the treatment of glaucoma** (column 3, line 66 to column 4, line 3 and column 5, lines 42-47), it anticipates the claims. Appellant states that Cherksey teaches that amiloride increases inflow, resulting in increased intraocular pressure. Column and line for this allegation has not been recited. Contrary to this allegation, Cherksey teaches

therapeutic benefits of amiloride, such as reduction of intraocular pressure (column 5, lines 25-46). Appellants' reliance on the post filing date reference, Avila et al., to allegedly provide evidence of Cherksey's failure to anticipate is not persuasive. The determination of anticipation or lack thereof must be based upon what was known in the art at the time the invention was made. Appellant makes unsupported allegations that Cherksey's patent is not enabled. Further, Appellants' statement that Cherksey neither mentions nor suggests that inhibiting or blocking NHE exchange would inhibit or reduce aqueous humor formation inflow or intraocular pressure is not germane to the rejection above. As stated above, the meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings." The instant specification teaches that "the modulators of the antiports are beta blockers, e.g., as timolol, amiloride analogs, e.g., amiloride or ethyl-isopropyl-amiloride and other compounds, e.g., cariporide." Where an explicit definition is provided by the Appellant for a term, that definition will control interpretation of the term as it is used in the claim. Cherksey teaches that amiloride is an agent that selectively blocks ion transport and interacts with a Sodium Hydrogen Exchange inhibitor at high concentrations (column 1, lines 21-27) and Amiloride and derivatives are capable of regulating membrane transport, cellular volume or cellular pressure disorders (column 2, lines 5-10). Further, the amiloride derivatives **are useful when applied topically for the treatment of glaucoma** column 3, line 66 to column 4, line 3 and column 5, lines 42-47), thus anticipating the claims. Alternatively stated, the Cherksey et al. teach administration of the same agent (amiloride and amiloride derivatives in the same manner, intraocularly,

serving the same functions, to regulate/reduce intraocular pressure for the treatment of Glaucoma.

Claims 94 and 102-105 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Drug Facts and Comparisons (1994).

Appellant asserts that timolol was not recognized by those knowledgeable in the field to be a NHE inhibitor. Where an explicit definition is provided by the Appellant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings."). Appellant argues that the reference offers no evidence that timolol achieved any inhibition of sodium-hydrogen antiport activity in the ciliary epithelial cells. In response, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. E.g., *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1351 (Fed. Cir. 2002); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where the result is a *necessary consequence* of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."); *Atlas Powder*, 190 F.3d at

1348-49 ("Because 'sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention. An inherent structure, composition, or function is not necessarily known."). In the instant case, the unappreciated anticipation of the properties of beta-blockers, such as timolol to inhibit sodium-hydrogen antiport activity while it is reducing intraocular pressure also does not require recognition. Appellant claims to have discovered the method of modulating aqueous secretion by modulating the antiports of the aqueous humor. Since the pharmaceutical compositions claimed by Appellant produced the claimed modulation of aqueous secretion, the discovery of the modulation of the antiport is inherent. In the context of the accidental anticipation, beta-blockers, such as timolol, do not accidentally modulate the antiport when the pharmaceutical composition is applied to a patient in need of treatment. The antiport necessarily and inevitably is modulated when the beta-blocker is applied and does not require a skilled artisan to recognize the inherent characteristic in the prior art that anticipates the claimed invention. Regarding administration Appellants asserts that the reference differs because it is not administered to the ciliary epithelial cells, however, the Examiner consulted the instant specification for information on how one would administer the NHE inhibitor (beta blocker) to the ciliary epithelial cell without administering an eye drop to the eye. The specification teaches that modulation compounds of the present invention can be administered opthamologically and also topically and preferably, administered to the eye topically (see page 18, lines 29-32). Drug Facts and Comparisons teach administration of beta blockers, such as timolol, to the eye ophthalmically for reduction

of intraocular pressure and treatment of glaucoma. It is not clear what is meant by Appellant's reference to "all things are inherent, because if you add enough links to what the inventors now disclose, there is nothing new under the sun". The Examiner will defer to the board to sort this out.

Claims 94-96, 99-110, 112 and 113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adorante et al. U.S. Patent No. 5,559,151 and Cherksey U.S. Patent No. 4,950,591.

In response to Appellant's argument that the references fail to show certain features of Appellant's invention, it is noted that the features upon which Appellant relies (i.e., bicarbonate-chloride exchange of the NPE cells) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant further asserts that Adorante fails to suggest administration of NHE/NHE1 inhibitors. In response, Appellant asserts that timolol was not recognized by those knowledgeable in the field to be a NHE inhibitor. Where an explicit definition is provided by the Appellant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a "lexicographic vacuum, but in the context of the specification and drawings."). Appellant defines the anion exchanger isoform 2 (AE2) as 4,4'-

diisothiocyanatostilbene-2,2'-disulfonate (DIDS) (see instant claims 99 and 100). Adorante et al. teach that DIDS treats glaucoma and/or ocular hypertension by inhibiting aqueous humor formation and thus, lowering IOP. Appellant again asserts that Cherksey teaches away from the invention, but this allegation is not grounded by the facts. Cherksey teaches amiloride and its derivatives for reduction of intraocular pressure. The nature of the problem to be solved, regulating intraocular pressure or regulating salt uptake or release by ciliary epithelial cells to modulate the aqueous humor would have led one of ordinary skill in the art to choose an appropriate agent to lower intraocular pressure and regulate salt uptake/release. Cherksey teaches that amiloride, (by Appellant's own definition is an NHE inhibitor) lowers intraocular pressure and Adorante et al. teach that DIDS (by Appellant's own definition is an AE2) lowers intraocular pressure and blocks chloride channels in the ciliary epithelium. Therefore, it would have been obvious to use both DIDS and Amiloride in combination to lower intraocular pressure and regulate salt uptake or release by the ciliary epithelium.

In response to Appellant's argument that the references fail to show certain features of Appellant's invention, it is noted that the features upon which Appellant relies (i.e., administering NHE/NHE1 inhibitors to the antiports) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 94-98, 102-110, 112 and 113 rejected under 35 U.S.C. 103(a) as being unpatentable over Brandt et al. U.S. Patent No. 5,585,401 and Cherksey U.S. Patent No. 4,950,591.

Appellant states that Brandt is irrelevant to Appellants invention because Dr. Civan (one of the inventors) and others have demonstrated that bumetanide is, by itself ineffective in lowering IOP. Appellant produces a reference that backs up this allegation. In response, Brandt et al. teach lowering of intraocular pressure with bumetanide. Every patent is presumed to be valid. 35 U.S.C. 282, first sentence. Public policy demands that every employee of the United States Patent and Trademark Office (USPTO) refuse to express to any person any opinion as to the validity or invalidity of, or the patentability or unpatentability of any claim in any U.S. patent, except to the extent necessary to carry out

(A) an examination of a reissue application of the patent,

(B) a reexamination proceeding to reexamine the patent, or

(C) an interference involving the patent.

The question of validity or invalidity is otherwise exclusively a matter to be determined by a court. Likewise, the question of enforceability or unenforceability is exclusively a matter to be determined by a court. See MPEP 1701 [R-3].

Regarding the Avila reference, Appellants' reliance on the post filing date reference to allegedly provide evidence of surprising results is not persuasive. The determination of obviousness or nonobviousness must be based upon what was known in the art at the time the invention was made. See 35 U.S.C. § 103: "A patent may not

be obtained…if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art". Appellant states that Cherksey's method of reducing intraocular pressure by administering amiloride is not Appellant's invention. Cherksey teaches amiloride and its derivatives for reduction of intraocular pressure. The nature of the problem to be solved, regulating intraocular pressure or regulating salt uptake or release by ciliary epithelial cells to modulate the aqueous humor would have led one of ordinary skill in the art to choose an appropriate agent to lower intraocular pressure and regulate salt uptake/release. Cherksey teaches that amiloride, (by Appellant's own definition is an NHE inhibitor) lowers intraocular pressure and Brandt et al. teach that bumetanide (by Appellant's own definition is an inhibitor of a Na+-K+-2Cl- symport) lowers intraocular pressure and blocks chloride channels in the ciliary epithelium. Therefore, it would have been obvious to combine bumetanide and amiloride in combination to lower intraocular pressure and regulate salt uptake or release by the ciliary epithelium.

Furthermore, the fact that Appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

Response to Declaration

The Declaration under 37 CFR 1.132 originally filed November 10, 2005, and resubmitted June 12, 2008 is insufficient to overcome the rejection of claims 94-110,

112, 113, 115 and 116 based upon the above rejection and because: Appellant claims that the class of molecules designated as NHE inhibitors did not include timolol or any other beta blocker at the time of the invention. In response, the Appellant identifies NHE inhibitors to include beta blockers and in particular, timolol in the instant specification (see page 6, lines 23-29, see also page 13, lines 11-26). A prior art reference may anticipate without disclosing a feature of the claimed invention, if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991). Beta blockers have been used for relief of intraocular pressure since at least 1980 (see Shell et al. U.S. Patent No. 4,281,654). The mere fact that they are not identified as NHE inhibitors does not detract from their actions of lowering intraocular pressure. Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. E.g., *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1351 (Fed. Cir. 2002); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where the result is a *necessary consequence* of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."); Atlas Powder, 190 F.3d at 1348-49 ("Because 'sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention. An inherent structure, composition, or function is not necessarily known."). In the instant case, the unappreciated anticipation also does not require recognition. Appellant's allegation that claim 94 does not embrace timolol or any other beta blockers is unfounded. Claim 94 is

drawn to regulating intraocular pressure with a composition comprising at least one sodium-hydrogen exchanger (NHE) inhibitor. When the Examiner looks to the instant specification to identify what Appellant means by NHE inhibitors, Page 6 of Appellant's instant specification identifies NHE inhibitors as beta-blockers (see at least page 6, lines 23-29, see also page 13, lines 11-26). Therefore, the scope of the declaration is not commensurate with the scope of the claim(s).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Donna Jagoe /D. J./

Conferees:

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611